

WEST Search History

DATE: Wednesday, March 19, 2003

<u>Set Name</u> side by side	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u> result set
	<i>DB=USPT; PLUR=YES; OP=ADJ</i>		
L1	6346411.pn.	1	L1
L2	5886151.pn.	1	L2
L3	rgd near5 antibod\$s	92	L3

END OF SEARCH HISTORY

L4 ANSWER 9 OF 56 MEDLINE
 TI Adhesion of sickle red blood cells and damage to interleukin-1 beta stimulated endothelial cells under flow in vitro.
 AU Natarajan M; Udden M M; McIntire L V
 SO BLOOD, (1996 Jun 1) 87 (11) 4845-52.
 Journal code: 7603509. ISSN: 0006-4971.
 AB Two factors that are hypothesized to contribute to vasoocclusive crises in sickle cell anemia are increased sickle red blood cell-endothelial cell interactions and damage to endothelium. Despite considerable study, the mechanisms by which erythrocyte-endothelial interactions occur and the role of endothelial damage have not yet been fully elucidated. In this report, we demonstrate that adhesion and damage may be related in a model of vasoocclusion in sickle cell anemia. Phase contrast microscopy coupled to digital image processing was used to determine the adhesion of sickle red blood cells to 1-, 4-, and 24-hour interleukin-I beta (IL-1 beta) stimulated endothelial cells in a parallel plate flow chamber. Morphological alterations to activated endothelial cells after the perfusion of sickle erythrocytes were also identified. Pretreatment of monolayers with 50 pg/mL of IL-1 beta for 1, 4, and 24 hours caused approximately 16-fold increases in adhesion of sickle cells to activated endothelium at all time points. Results with an Arginine-glycine aspartic acid (RGD) peptide and monoclonal **antibodies** indicated a role for three different endothelial cell receptors: alpha v beta 3 after 1 hour of IL-1 beta stimulation; E-selectin after 4 hours of IL-1 beta stimulation; and vascular cell adhesion molecule-1 after prolonged exposure to cytokines. Perfusion of sickle, but not normal, erythrocytes resulted in alteration of endothelial morphology. Approximately 6% to 8% damage was observed on 4- and 24-hour IL-1 beta stimulated endothelial cells after the perfusion of sickle cells. Damage to 24-hour activated endothelial cells showed a positive correlation ($r = .899$) with the number of adherent sickle erythrocytes.

L4 ANSWER 22 OF 56 MEDLINE
 TI Engineered idiotypes. Immunochemical analysis of antigenized antibodies expressing a conformationally constrained Arg-Gly-Asp motif.
 AU Rossi F; Billetta R; Ruggeri Z; Zanetti M
 SO MOLECULAR IMMUNOLOGY, (1995 Apr) 32 (5) 341-6.
 Journal code: 7905289. ISSN: 0161-5890.
 AB We report on the immunochemical characterization of two **antibodies** engineered to express RGD, a peptide from adhesive proteins of the extracellular matrix. One or three RGD motifs were introduced in the third complementarity-determining region (CDR) of a murine heavy (H) chain variable (V) region gene yielding two antibodies, gamma 1RGD and gamma 1(RGD)3. A murine monoclonal antibody (mAb) raised against an RGD-containing synthetic peptide bound in Western blot the H chain of both gamma 1RGD and gamma 1(RGD)3. Pronectin F, a genetically-engineered polymer containing RGD, abrogated this binding. Anti-idiotypic **antibodies** against the (RGD)3 loop were generated in a rabbit by immunization with gamma 1(RGD)3. Anti-idiotypic **antibodies** purified by affinity-chromatography on the synthetic peptide GRGDSPC reacted in ELISA with gamma 1(RGD)3 and human fibronectin. Adhesive proteins, unlike RGD-containing synthetic peptides, were able to interfere with the interaction between gamma 1(RGD)3 and the anti-idiotypic antibodies. These results suggest that it is possible to genetically engineer the hypervariable loops of immunoglobulins and confer them new idiotypic characteristics. These results support the concept of antibody mimicry.

L4 ANSWER 36 OF 56 MEDLINE
 TI Expression of conformationally constrained adhesion peptide in an antibody CDR loop and inhibition of natural killer cell cytotoxic activity by an

antibody antigenized with the **RGD** motif.

AU Zanetti M; Filaci G; Lee R H; del Guercio P; Rossi F; Bacchetta R;
Stevenson F; Barnaba V; Billetta R

SO EMBO JOURNAL, (1993 Nov) 12 (11) 4375-84.

Journal code: 8208664. ISSN: 0261-4189.

AB We report that an antibody engineered to express three Arg-Gly-Asp (RGD) repeats in the third complementarity-determining region of the heavy chain (antigenized antibody) efficiently inhibits the lysis of human erythroleukemia K-562 cells by natural killer (NK) cells. Synthetic peptides containing RGD did not inhibit. Inhibition was specific for the (RGD)₃-containing loop and required simultaneous occupancy of the Fc receptor (CD16) on effector cells. The antigenized antibody inhibited other forms of cytotoxicity mediated by NK cells but not cytotoxicity mediated by major histocompatibility complex-restricted cytotoxic T lymphocytes (CTL). A three-dimensional model of the engineered antibody loop shows the structure and physicochemical characteristics probably required for the ligand activity. The results indicate that an RGD motif is involved in the productive interaction between NK and target cells. Moreover, they show that peptide expression in the hypervariable loops of an antibody molecule is an efficient procedure for stabilizing oligopeptides within a limited spectrum of tertiary structures. This is a new approach towards imparting ligand properties to antibody molecules and can be used to study the biological function and specificity of short peptide motifs, including those involved in cell adhesion.

L4 ANSWER 38 OF 56 MEDLINE

TI Isolation of leukocyte response integrin: a novel RGD-binding protein involved in regulation of phagocytic function.

AU Carreno M P; Gresham H D; Brown E J

SO CLINICAL IMMUNOLOGY AND IMMUNOPATHOLOGY, (1993 Oct) 69 (1) 43-51.

Journal code: 0356637. ISSN: 0090-1229.

AB We have described previously an adhesive protein on neutrophils (PMN) which recognizes fibrinogen, fibronectin (Fn), von Willebrandt's factor, vitronectin, collagen, and synthetic peptides containing the Arg-Gly-Asp (RGD) sequence (Gresham et al., J. Cell Biol. 108, 1935-1943, 1989). We have called this oligospecific receptor the leukocyte response integrin (LRI). Engagement of LRI leads to both increased ingestion via PMN IgG Fc receptors and to adhesion and chemotaxis to certain extracellular matrix proteins. Now, we have purified an RGD-binding receptor from DMSO-differentiated HL-60 cells (dHL-60) by peptide affinity chromatography which has the biochemical, immunologic, and functional characteristics of LRI. The purified protein contains two bands of 135 and 90 kDa under nonreducing conditions SDS-PAGE. Immunologic characterization of the dHL-60 RGD receptor showed that, by Western blot and ELISA, the lower M(r) band was recognized by mAb 7G2, raised against placental beta 3, which is known to inhibit LRI function. However, despite this functional and immunologic cross-reactivity with beta 3, the receptor was not recognized efficiently by a polyclonal **antibody** to placental **RGD**-binding proteins, predominantly alpha v beta 3. Moreover, polyclonal antibody raised to the dHL-60 receptor (Ab1) did not react with placental RGD-binding proteins. By immunoprecipitation or ELISA, we demonstrated that the purified RGD-binding receptor was not alpha IIb beta 3 or alpha v beta 3 and did not contain the integrin chains alpha 4, beta 2, or beta 7. Functionally, Ab1 totally inhibited Fn-stimulated ingestion by PMN. Moreover, Ab1 inhibited phagocytosis stimulated by the peptide KGAGDV, which is the most specific ligand for LRI currently known, and Ab1 inhibited the binding of KGAGDV-coated microspheres to PMN and monocytes. FACS analysis with Ab1 showed staining of monocytes, PMN, and lymphocytes but not platelets or erythrocytes. We conclude that LRI is a novel RGD-binding receptor which exists on leukocytes and which shares an antigenic epitope(s) with beta 3. This receptor recognizes multiple

RGD-containing ligands and can mediate signal transduction for adhesion, chemotaxis, and activation of increased phagocytic potential by PMN and monocytes.

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